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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/821,832	03/30/2001	Thomas Tuschl	0399.2008-002	6240

23628 7590 01/07/2005

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/821,832	TUSCHL ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-109* is/are pending in the application.

4a) Of the above claim(s) *6-11,13-15,17-41,44-47,51-71 and 96-102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,12,16,42,43,72-95 and 103-109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/28/04; 7/25/03; 12/6/02; 4/12/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the office action and amendment filed on October 26, 2004 has been entered.

Status of the application

2. New claims are 103-109 are added. Claims 48-50 are cancelled. Claims 1-5, 12, 16, 42-43, 72-95, 103-109 are considered for examination. Claims 6-11, 13-15, 17-41, 44-47, 51-71, 96-102 are withdrawn.

3. This application is filed on March 30, 2001 and claims benefit of US provisional applications 60/265,232 filed on 1/31/2001 and 60/193,594 filed on 3/30/2000.

New grounds of rejections necessitated by Amendment

Claim Rejections - 35 USC § 112

4a. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 12, 16, 42-43, 72-95, 103-109 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claims are drawn to an isolated RNA or DNA of from about 21 to about 23 nucleotides that has sequence corresponding to an mRNA and mediates RNA interference by direct cleavage of the mRNA mRNA to which it corresponds, and calms are also drawn to variants of an isolated RNA which vary by addition, substitution or alteration of one or more

nucleotides and a pharmaceutical composition comprising said isolated RNA and DNA. The specification fails to provide structural limitations of said isolated RNA and DNA except for a length ranging from 21 to about 23 nucleotides. Further the specification fails to provide any information regarding the cleavage site of the mRNA to which the isolated RNA corresponds to. The large genus of variants is represented in the specification by the broad term "modified analog". Thus, applicants have expressed possession of only one species in a genus, which comprises hundreds of millions of different possibilities. The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common elements or attributes of the structural information (sequences) are disclosed. With regard to the isolated RNA, it is insufficient to demonstrate identity of regulatory activity in mRNA and cleavage site for its action (mediates RNA interference) where no structural information regarding where in the RNA the activity resides. Further no information is given regarding a methodology to determine such common elements or attributes. Further, there is no description of variants.

With regard to the written description, all of the claims drawn to an RNA or an analog of isolated RNA, or an isolated DNA encoding said RNA, encompass different structural limitations, for which, no structural limitation is provided in the specification. It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that "...if inventor is unable to

envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that: "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In this application at the time of filing, there is no record or description, which would demonstrate conception or written description of any structural information of isolated RNA or an analog of an isolated RNA or isolated DNA encoding said RNA with retaining correlative function in the claimed product.

4b. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 4, 79, and 89 recites the limitation "the analog". There is insufficient antecedent basis for this limitation in the claim. The instant claims lack support for this limitation because the independent claims upon which these claims are dependent lack support for this limitation.

B. Claim 12 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are confusing and unclear because it is unclear whether the claims are drawn to a product or a process.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

A. Claims 76-95, 106-109 are rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al. (US 6,506,559).

Fire et al. teach an isolated double-stranded RNA of claim 76, 86, of at least 25 nucleotides, (which comprise RNA from about 21 to about 23 nucleotides) that mediate RNA interference of an mRNA to which it corresponds (column 4, lines 23-28, 41-53, column 7, lines 42-52, column 8, lines 1-6, column 14, lines 44-67, column 15, lines 1-30);

With regard to claim 77, 87, Fire et al teach that the RNA comprises 3' terminal hydroxyl group (ribonucleotides) (see column 4, lines 41-46);

With regard to claim, 80, 90, Fire et al. teach that the said RNA inactivates a corresponding gene by transcriptional silencing (see column 6, lines 44-67, column 7, lines 1-52);

With regard to claims 78-79, 88-89, Fire et al. also teach that the RNA comprises chemically synthesized or analog which differs from RNA by addition, deletion, substitution or alteration (see column 7, lines 53-67);

With regard to claim 81, Fire et al. teach a pharmaceutical composition comprising said double-stranded RNA and an appropriate carrier (see column 14, lines 17-31);

With regard to claim 86, 91, Fire et al. teach that isolated RNA is obtained from double-stranded RNA that has been cleaved into sense and antisense fragments of about 21 to about 23 nucleotides (see column 15, lines 10-30, lines 57-61).

With regard to claims 82- 84, 92-94, Fire et al. also disclose isolated DNA comprising DNA encoding said double-stranded RNA (see column 20, lines 19-25, table. 1);

With regard to claims 85, 95, Fire et al. also teach that the DNA encoding said RNA is processed from eukaryotic cells and result in RNA segments of a protein degradation (see column 20, lines 26-40).

With regard to claims 106-109, Fire et al. teach that said RNA is complementary to the mRNA, or the gene that is derived from human, or mammal (see col. 8, line 36-38).

Thus the disclosure of Fire et al. meets the limitations in the instant claims.

B. Claims 1, 3-5, 12, 16, 42, 48-50, 76, 78-86, 88-95, 103-107 are rejected under 35 U.S.C. 102(e) as being anticipated by Baulcombe et al. (USPN. 6,531,647).

Baulcombe et al. teach an isolated RNA of claim 1, 12, 16, 76, of about 14 to 23 nucleotides , (which comprise RNA from about 21 to about 23 nucleotides) that mediates RNA interference of an mRNA to which it corresponds (see column 7, lines 38-44, column 6, lines 40-45, column 12, lines 47-53);

With regard to claim 5, 80, 90, Baulcombe et al. teach that the said RNA inactivates a corresponding gene by transcriptional silencing (see column 5, lines 33-52, column 6, lines 10-21);

With regard to claims, 1, 76, Baulcombe et al. et al. also teach that the RNA is a double-stranded RNA or single-stranded (see column 6, lines 40-45);

With regard to claims 3-4, 78-79, 88-89, 103-107, Baulcombe et al. also teach that the isolated RNA comprises chemically synthesized or naturally occurring analog which differs from RNA by addition, deletion, substitution or alteration (see column 6, lines 40-45, column 12, lines 47-53);

With regard to claim 86, 91, Baulcombe et al. teach that isolated RNA is obtained from double-stranded RNA that has been cleaved into sense and antisense fragments of about 21 to about 23 nucleotides (see column 6, lines 40-45, column 7, lines 6-20).

With regard to claims 42, 82- 84, 92-94, Baulcombe et al. also disclose isolated DNA comprising DNA encoding said double-stranded RNA (see column 11, lines 60-63, column 12, lines 47-53);

With regard to claims 85, 95, Baulcombe et al. also teach that the DNA encoding said RNA is processed from eukaryotic cells and result in RNA segments of a protein degradation (see column 7, lines 6-20).

Thus the disclosure of Baulcombe et al. meets the limitations in the instant claims.

Response to Arguments

6. Applicant's response to the office action is fully considered and is found persuasive in part.

7. With regard to the status of the pending claims, applicants' arguments regarding claims 42 and 43 are considered and Examiner notes that in the previous office action both 42 and 43 are considered for examination and hence Examiner reiterates that these two claims are treated as pending and being examined.

8. With reference to the rejection made in the previous office action under 35 USC 112, first paragraph, Applicants' arguments are fully considered and found not persuasive. Applicants argue that the instant claims are amended to include the binding specificity of the RNA and satisfies the written description requirement under 35 USC 112, first paragraph. Applicants' arguments are fully considered and found not persuasive because, the new limitation "has sequence correspondence to an mRNA" and mediates RNA interference "by direct cleavage of the mRNA" to which it corresponds, does not provide any information regarding the structure of the RNA that has sequence corresponding to an mRNA and to the cleavage site in the mRNA to which the isolated RNA corresponds to. The claims broadly recites any mRNA which corresponds to the isolated RNA, for which the specification lacks support for these large number of mRNA sequences with no structural limitations (start and end points) and no support for the cleavage site in the recited mRNA. Applicants also argue that the size and complementarity are sufficient for a person of ordinary skill in the art to practice the invention and assert the that the RNAi technology is well known in the scientific field as exemplified by the state of art and commercial use.

Applicants' arguments are fully considered and found unpersuasive because the claims are rejected under lack of written description, but not under a utility or enablement rejection. The broadly recited sequence correspondence with an mRNA does not satisfy the structural limitations of the claimed RNA. The sequence corresponding to an mRNA does not provide any evidence whether the sequence interferes with RNA transcription or not, especially because the transcriptional start site is not disclosed.

Applicants further argue that the claimed RNA and DNA molecules have common structural features and no need to be defined by sequence and assert that the instant claims (1-5, 12, 16, 43, 76-81, 86-91, 103-109) are drawn to RNA not DNA sequences. Applicants' assertions are fully considered and found not persuasive. The instant claims are drawn to RNA and fragments or analogs of RNA varying by deletion substitution or alteration of one or more nucleotides, thus each of these variants would have a structure that is different from the other, for which the specification has not provided any structural limitations to identify which of these RNA fragments are structurally similar or different. The corresponding DNA, which encodes such RNA molecule, would also differ in its structure. Thus the structure which is dependent on a sequence is required, which is not provided in the instant specification.

Applicants also argue that the claims are amended to delete the term analog to narrow the scope of the claims. However, examiner notes that the dependent claims 4, 79, 89 recite fragments or analogs vary by addition, substitution or alteration of one or more nucleotides. Thus the specification lacks support for this large number of fragments. Therefore the rejection is maintained and rewritten as above, to include new claims.

9. With regard to the rejection under 35 USC 102(e) as being anticipated by Fire et al. Applicants' arguments are fully considered and found not persuasive. Applicants argue that Fire et al. teach nucleic acids of length of at least 25nucleotides and does not teach nucleic acids that are about 21 to about 23 nucleotides in length. Applicants' arguments are fully considered and found not persuasive because the term "about" is a relative term and do not limit the length of nucleotides. Thus the limitation "about 21 to about 23" includes a relative length of nucleotides around 21 to 23, that is, it can include 18, or 19, or 20, or 24 or 25 or 26 nucleotides in length. Therefore Fire et al. does anticipate the instant claims and the rejection is maintained and rewritten to include new claim limitations.

10. With regard to the rejection under 35 USC 102(e) as being anticipated by Baulcombe et al., Applicants' arguments are fully considered and found not persuasive. Applicants argue that Baulcombe et al. teach nucleic acids of length ranging from 14 to 300 nucleotides and does not teach nucleic acids that are about 21 to about 23 nucleotides in length. Applicants' arguments are fully considered and found not persuasive because as discussed above the term "about" is a relative term and do not limit the length of nucleotides. Further the nucleic acid length ranging from 14-300 nucleotides taught by Baulcombe et al. does include the claimed nucleic acid length from about 21 to about 23 nucleotides. Therefore Baulcombe et al. does anticipate the instant claims and the rejection is maintained.

10. With regard to the rejection made in the previous office action under 35 USC 102(e) as being anticipated by Morrisey et al., Applicants' arguments are fully considered and found persuasive. Thus the rejection is withdrawn in view of persuasive arguments.

11. With regard to the rejection made in the previous office action under 35 USC 103(a), Applicants' arguments and amendment are fully considered and the rejection is withdrawn in view of the amendment.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone numbers for the organization where

this application or proceeding is assigned are 703-872-9306 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
January 5, 2005

JEFFREY FREDMAN
PRIMARY EXAMINER
1/5/05